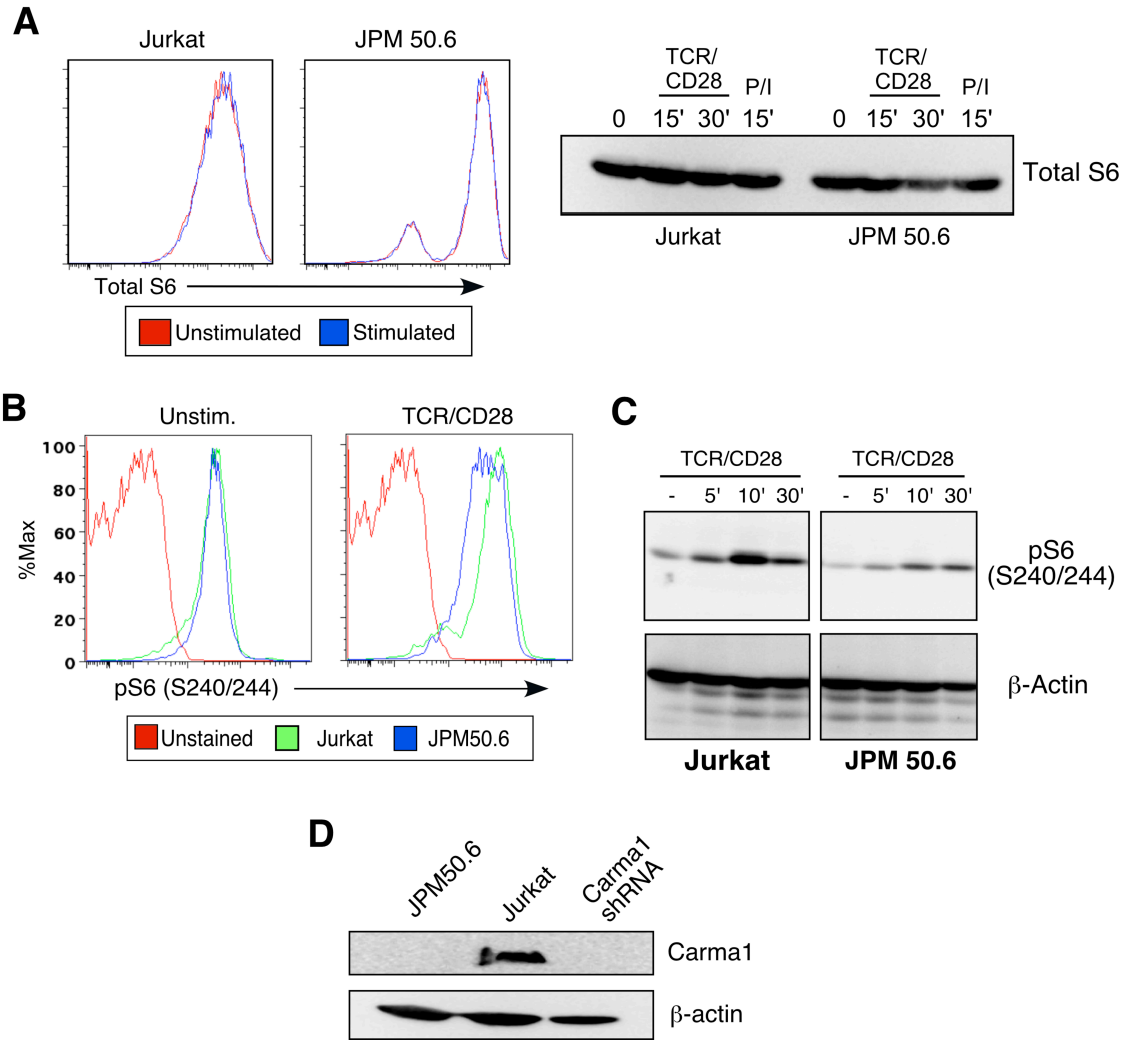

Fig. S1. Analysis of total S6 and Carma1 protein abundance in parental and mutant Jurkat cell lines. (**A**) Jurkat cells and JPM 50.6 cells were left unstimulated or were stimulated with anti-CD3 and anti-CD28 antibodies (TCR/CD28) or with PMA and ionomycin (P/I). Left: Cells were analyzed by flow cytometry for total S6 protein. Right: Cell lysates were analyzed by Western blotting with antibody against total S6 protein. (**B**) Jurkat cells and JPM 50.6 cells were left unstimulated or were stimulated with anti-CD3 and anti-CD28 antibodies before being analyzed by flow cytometry for pS6. (**C**) Jurkat cells and JPM 50.6 cells were left unstimulated or were stimulated with anti-CD3 and anti-CD28 antibodies before being analyzed by Western blotting with antibodies against the indicated proteins. (**D**) JPM 50.6 cells, Jurkat cells, and Jurkat cells transduced with lentivirus expressing Carma1-specific shRNA were analyzed by Western blotting with antibodies against the indicated proteins. Results shown in each panel are representative of three independent experiments.

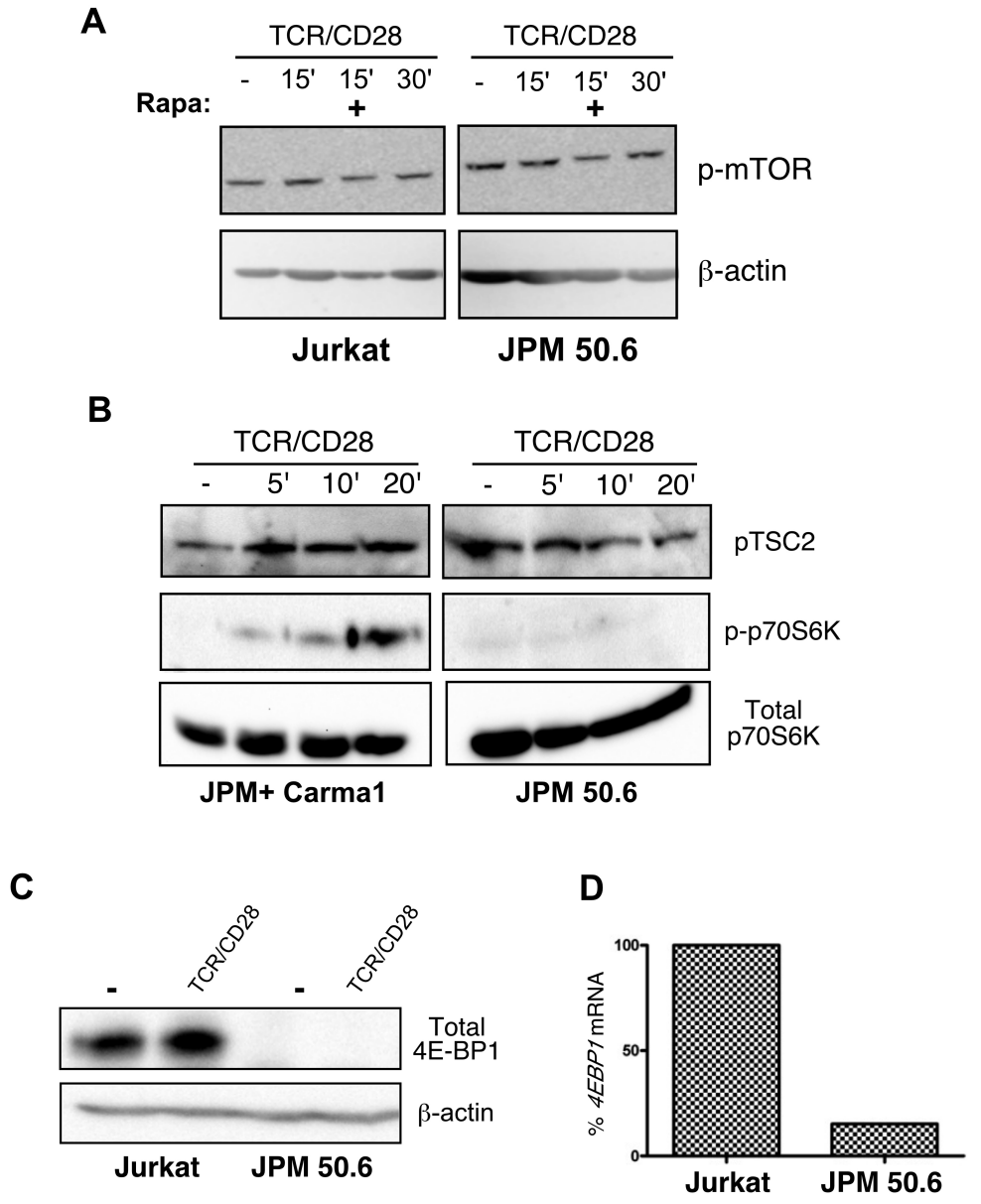

Fig. S2. Analysis of mTOR and TSC phosphorylation and of 4E-BP1 abundance in Carma1-deficient cells. (**A**) Parental Jurkat cells (left) and Carma1-deficient JPM 50.6 cells (right) were stimulated with anti-CD3 and anti-CD28 antibodies for the indicated times. For the 15-min time point, cells were incubated in the absence or presence of 100 nM rapamycin (Rapa). Cell lysates were then analyzed by Western blotting with antibodies against the indicated proteins. (**B**) Carma1-reconstituted JPM50.6 and parental JPM 50.6 cells were stimulated with anti-CD3 and anti-CD28 antibodies for the indicated times. Cell lysates were analyzed by Western blotting with antibodies against the indicated proteins. (**C** and **D**) Jurkat cells and JPM 50.6 cells were analyzed by (C) Western blotting to detect total 4E-BP1 protein, and (D) qRT-PCR to determine the relative amounts of 4E-BP1 mRNA. Data shown are representative of either three (panels A and B) or two (panels C and D) independent experiments.

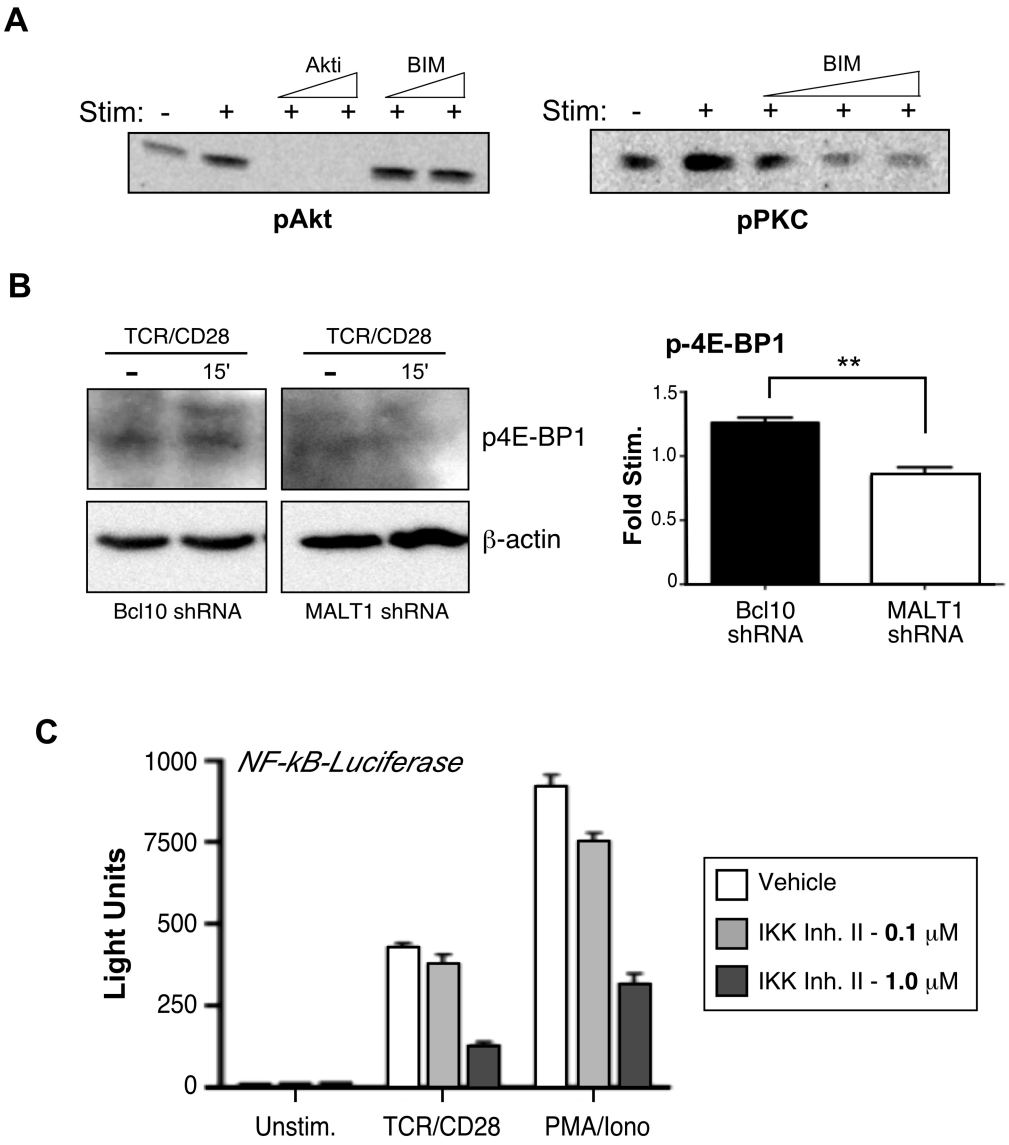

Fig. S3. Specificity of kinase inhibitors and comparison of the extent of 4E-BP1 phosphorylation in T cells lacking either Bcl10 or MALT1. (**A**) Jurkat cells were left untreated or were pretreated with 10 or 20 μM Akti1/2 or 500 nM or 1 μM BIM before being stimulated with anti-CD3 and anti-CD28 antibodies for 15 min. Cell lysates were then analyzed by Western blotting for pAkt S473 (left) and pPKCθ (right). (**B**) Bcl10shRNA cells and MALT1shRNA cells were left untreated or were stimulated with anti-CD3 and anti-CD28 antibodies for 15 min. Cell lysates were then analyzed by Western blotting for p4E-BP1. Right: Densitometric analysis of the fold-increase in p4E-BP1 abundance in the indicated stimulated cells relative to that in unstimulated cells. (**C**) Jurkat cells were pretreated with vehicle or the indicated concentrations of IKK inhibitor II, and then were stimulated with anti-CD3 and anti-CD28 antibodies or with PMA and ionomycin for six hours. Samples were then analyzed for NF-κB luciferase reporter activity. Data in each panel are representative of three independent experiments.

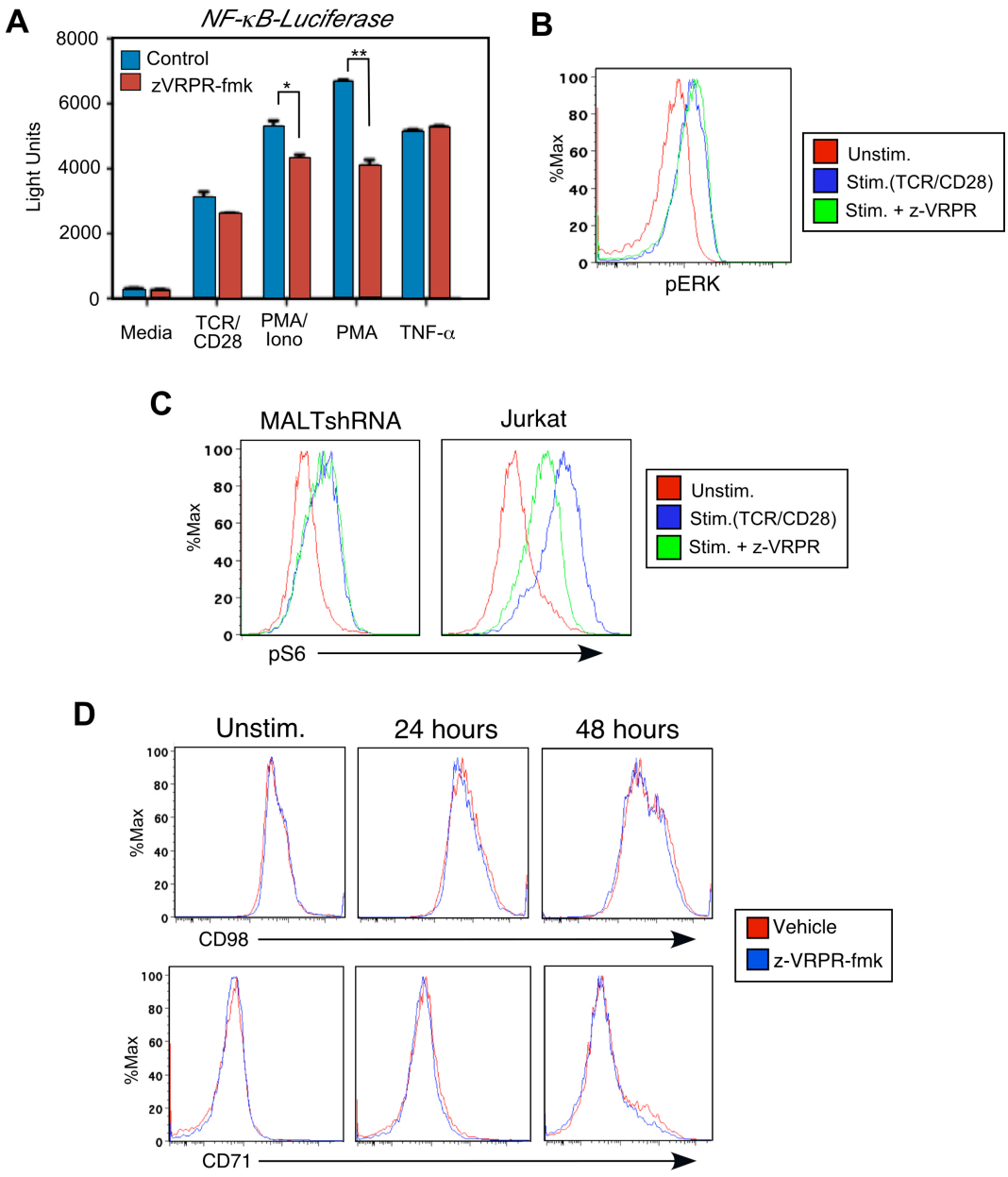

Fig. S4. The MALT1 inhibitor z-VRPR-fmk has a limited repertoire of effects on T cell activation. (**A**) Jurkat T cells pretreated with vehicle or 75 μM z-VRPR-fmk were stimulated with anti-CD3 and anti-CD28 antibodies, PMA and ionomycin, or rhTNF-α for 6 hours. NF-κB luciferase reporter assays were then performed. (**B**) Jurkat cells were pretreated with vehicle or z-VRPR-fmk before being stimulated with anti-CD3 and anti-CD28 antibodies, and then were analyzed by flow cytometry for pERK. (**C**) Jurkat cells and MALT1shRNA cells were pretreated with vehicle or z-VRPR-fmk and then were stimulated with anti-CD3 and anti-CD28 antibodies. Cells were then analyzed by flow cytometry for pS6. (**D**) Primary mouse $CD4^+$ T cells were stimulated with anti-CD3 and anti-CD28 antibodies in the presence or absence of z-VRPR-fmk for the indicated times and then were analyzed by flow cytometry to determine the cell-surface abundance of CD98 (top) and CD71 (bottom). Data in each panel are representative of three (panels A, B and D) or two (panel C) independent experiments.